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PATHOLOGICAL SUB-TYPES, RISK FACTORS AND OUTCOME OF STROKE AT THE NAIROBI HOSPITAL, KENYA

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ABSTRACT

Background: Stroke is one of the most common causes of morbidity and mortality the world over. Established risk factors such as arterial hypertension, diabetes mellitus, cigarette smoking, hyper-lipidaemia, micro-vascular rupture, male gender, age and observed co-morbidities such as sickle cell disease, HIV/AIDS infection and cerebral malaria are increasingly being encountered in the tropics.

Objectives: To determine pathological sub-types, risk factors, in-hospital period prevalence and in-hospital outcome of stroke.

Design: Hospital-based retrospective study.

Setting: The Nairobi Hospital, Nairobi, Kenya.

Subjects: Patients with recorded diagnosis of stroke/cerebral vascular accident; as per WHO criteria for diagnosis of stroke, all gender and age ≥ 18 years were studied.

Results: A total of 2629 patients were admitted to the division of medicine at the hospital during study period. Eighty patients had diagnosis of stroke; giving an in-hospital period prevalence of 3042/100,000. Mean age was 61.3 years, mode; 63 years, range 34-95 years. Males were 43 (53.8%), M to F ratio 1.2:1 stroke sub-types: Ischaemic stroke 68(85%), haemorrhagic stroke seven (8.8%). In five patients (6.3%) no evidence of stroke sub-type was on-record. Established risk factors for stroke included hypertension and diabetes mellitus. Hypertension was found in 64 patients (80%) and diabetes-mellitus in 27(33.7%). Twenty three patients (28.8%) had both hypertension and diabetes-mellitus. Co-morbidities were observed and included mitral-stenosis, cardiac-arrhythmias cardio-myopathy, HIV/AIDS, Left Ventricular Hypertrophy (LVH), infective endocarditis, atrial septal aneurysm, carotid plaques with or without stenosis and hyper-homocystenemia. Mean hospital stay was 12.5 days; range 22-70 days. Seventy five patients (93.8%) were discharged and four (5%) died in hospital. All patients who died had anterior circulation ischaemic stroke as per Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.

Conclusion: Ischaemic stroke is the most common pathological sub-type observed in this study. Hypertension is the leading observed risk factor for stroke. Hospital period prevalence for stroke of 3042/100,000 was found. Seventy five patients (93.8%) were discharged and four (5%) died in hospital.

INTRODUCTION

Clinicians in the developing countries are increasingly encountering and managing patients with stroke. Stroke has for a long time been thought to be a problem of the developed countries only, however, it is becoming an epidemic in tropical countries with frequencies estimated at 35/100,000 and 183/100,000 in South America (1). A hospital based study in Tanzania by Matuja *et al* (2) indicated

that 60% of patients studied had haemorrhagic stroke and 39.9% had ischaemic stroke. The risk factors identified were hypertension and diabetes mellitus. Rural community prevalence studies in South Africa (3) give rates of 243-300/100,000 and that 66% of stroke patients were totally dependent on care. Lack of diagnostic facilities such as neurological imaging (CT/MRI Scan) does hinder appropriate documentation of stroke sub-types in resource poor countries.

Stroke is one of the most common causes of morbidity and mortality the world over (4). Countries centred on the equator have a large burden of cerebral vascular diseases (4, 5). Established risk factors such as arterial hypertension, diabetes mellitus, cigarette smoking, hyper-lipidaemia, micro-vascular rupture, male gender, age and observed co-morbidities such as sickle cell disease, HIV / AIDS infection, hyper-homocystenemia and cerebral malaria are increasingly being encountered in the tropics. Some of these new developments are largely due to urbanisation and change to unhealthy dietary and lifestyle habits (5-14).

In the developing world, stroke appears to be seen more amongst the youth as compared to the western developed world (15, 16). Our population predominantly comprises the youth; therefore there is even greater need to systematically evaluate the prevalence and risk factors of stroke locally. Stroke has high morbidity and mortality rates and causes heavy burden on health delivery system that is already choked by a myriad of infections, malnutrition and water-borne diseases. Stroke is preventable and addressing risk factors would go a long way in managing the problem. Stroke is the major neurological cause of hospital admission in Nigeria (17). In Senegal, it is the third most common cause of admission to neurological services and consumes close to 40% of healthcare resources (18). Stroke is defined clinically as a focal or global disturbance of cerebral function of sudden onset lasting 24 hours or longer or leading to death with no apparent cause other than that of vascular origin (19, 20).

Pathological sub-types of stroke include cerebral infarction, intra-cerebral haemorrhage and sub-arachnoid haemorrhage. There are, however, a small percentage of undetermined sub-types (21, 22).

Stroke incidence and prevalence studies in sub-Saharan Africa are scarce. Most studies are hospital based. These studies have tried to highlight risk factors and burden of stroke in their respective geographical locations. Matenga (23) in a Zimbabwean community prospective incidence study gives a crude incidence rate of stroke at 30.7/100,000. Njamnishi, *et al* (24) in Cameroon showed that chronic Chlamydia pneumonia infection is associated with ischaemic stroke. Zenebe *et al* (25) in an urban hospital based study in Ethiopia showed the following risk factors for strokes; hypertension 65.6%; cardiac diseases 27.7% and valvular heart disease 40%. Kumwenda *et al* (26) in a similar study in Malawi showed that HIV / AIDS infection was a major risk factor for ischaemic stroke comprising 58% of the patients studied.

From the foregoing, it is apparent that risk factors for stroke may be varied in sub-Saharan Africa and

requires intensive research. No similar studies have been done locally in Kenya.

The burden of stroke is increasing in sub-Saharan Africa considering other myriad of medical problems. Njoh (27) found that stroke was the second most common cause of hospital admissions in Liberia. Walker *et al* (16) in Gambia found that 27% of patients with stroke died in the first month of hospitalisation and 44% were dead by six months. Advanced age is a key determinant of morbidity and mortality in stroke. Older people are at much greater risk of death, this may reflect lack of adequate care for elderly patients with stroke (28). Tropical diseases such as malaria and sickle-cell disease are major co-morbidities of ischaemic stroke with resultant morbidity and mortality as found by Obama *et al* (29) in Cameroon.

What is the situation in Kenya? There are no similar studies done locally to map the demography, risk factors and burden of stroke. Prospective hospital-based studies are needed; followed by high quality stroke incidence and prevalence studies in various centres in the country.

It is for this reason that we found it prudent to start with a retrospective urban hospital based study to try and document the sub-types, risk factors, co-morbidities, in-hospital point prevalence and in-hospital outcome of stroke.

Primary objective: To determine the pathological sub-types, established risk factors; in-hospital point prevalence, observed co-morbidities and in-hospital outcome of stroke.

Secondary objectives: To determine age, gender and neuro-imaging findings.

Study design: Hospital based retrospective observational study.

MATERIALS AND METHODS

Case definition: Clinically, stroke was defined as per WHO criteria: Topical or global disturbance of cerebral function of sudden onset lasting 24 hours or longer with no apparent cause other than that of vascular origin (19).

Inclusion criteria: Patients with recorded diagnosis of stroke / cerebral vascular accident; as per WHO criteria for diagnosis of stroke, all gender and age ≥ 18 years.

Exclusion criteria:

- (i) Absence of neuro-imaging on record (minimum required is Brain CT and / or MRI Scan)
- (ii) Patients with transient ischaemic attacks that is, symptoms lasting less than 24 hours with complete resolution as on record.

All consecutive medical file records of patients admitted to The Nairobi Hospital (Division of Medicine) between January 2003 and June 2006 with diagnostic category of stroke/cerebral vascular accident was scrutinised.

All the files were personally scrutinised and records taken by both authors. The total number of all patients admitted to the division of medicine during the same study period was noted.

Definition of variables: Diabetes Mellitus 29, Hypertension 30, Hyper-lipidemia.; classification as per NCEP/ATP III guidelines 31.

Data processing and statistical analysis: Data were handled with confidentiality and codes were used to record data. The data were verified and cleaned. Statistical analysis was done using SPSS 10.0 software. Analysis was done by descriptive statistics e.g. mean, median, mode for continuous variables and frequency distribution for categorical variables.

Ethical consideration: Permission for the study was sought from The Nairobi Hospital Ethics and Research Committee. The patients' file records were coded and confidentiality maintained on information found therein.

RESULTS

A total of 2629 patients were admitted to the Nairobi Hospital in the Division of Medicine during the study period of January 2003 and June 2006. Eighty of these patients were identified to have stroke as per the inclusion criteria. This gives an in-hospital period prevalence of 3042/100,000 for stroke.

Age distribution: The patients had a mean age of 61.3 years, mode of 63 years with a range of 34 to 95 years.

Gender distribution: Males comprised 43 (53.8%) and females 37 (46.3%) of the patients this gives an M: F ratio of 1.2:1.

Sub-types of stroke: Stroke sub-types comprised; ischaemic stroke 68 patients (85%) and haemorrhagic stroke seven patients (8.8%). In five (6.3%) patients there was no record of stroke sub-type on file, though it was recorded in the notes that neuro-imaging was done and was consistent with stroke (Figure 1).

Of the 68 patients with ischaemic stroke; 43 (63%) had anterior circulation (anterior cerebral artery and middle cerebral artery that is, large-artery atherosclerosis) ischaemic lesions on CT/MRI scans; four patients (5.9%) had posterior circulation (that is, large-artery atherosclerosis) ischaemic lesions on

CT/MRI scans and 21 patients (30.9%) had brainstem lacunae (that is, small vessel occlusion) ischaemic lesions on CT/MRI scans (Figure 2). Seven patients (8.8%) had haemorrhagic stroke. Five of these patients had arterial hypertension, one had diabetes mellitus and one had very high (>4.9 ml/l) LDL cholesterol as associated risk factors.

Figure 1
The different sub-types of stroke

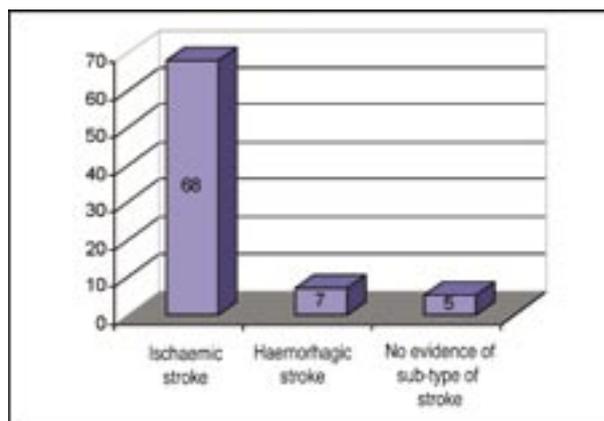
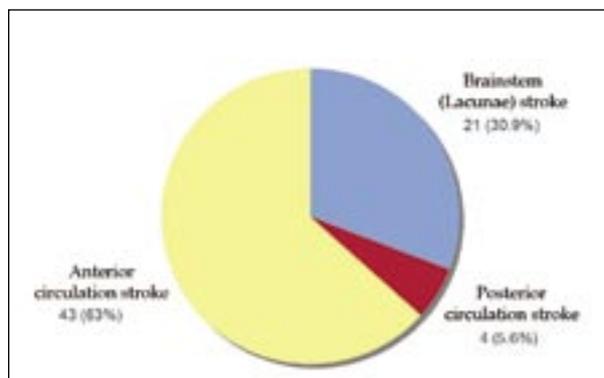


Figure 2
The TOAST classification of sub-type of acute ischaemic stroke

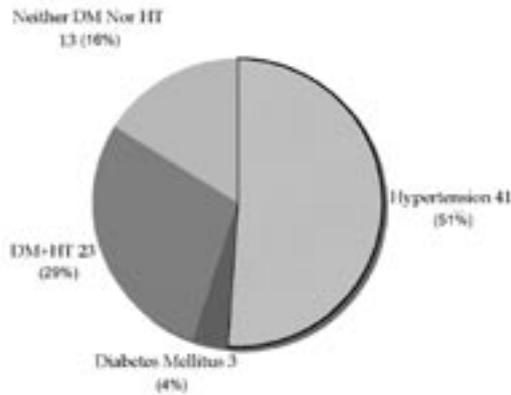


ESTABLISHED RISK FACTORS OBSERVED

Arterial hypertension: Forty one (51%) patients had hypertension alone, 23 patients had co-morbidity of hypertension and diabetes mellitus. Overall hypertension was seen in 64 (80%) patients.

Diabetes mellitus: Only three patients had isolated diabetes mellitus. Twenty three patients had both diabetes mellitus and hypertension. Thirteen (16%) patients had neither hypertension nor diabetes mellitus (Figure 3).

Figure 3
The proportion of risk factors of hypertension and diabetes mellitus



Co-morbidities observed: Co-morbidities were observed and these included mitral-stenosis, cardiac-arrhythmias cardio-myopathy, HIV/AIDS, LVH, infective endocarditis, atrial septal aneurysm, carotid plaques with or without stenosis, hyper-homocystenemia and anaemia.

Forty eight patients (60%) had trans-thoracic 2D echo-cardiograms done. Of these 48 patients; 25 (52%) had left ventricular hypertrophy; 13 (27.7%) had normal ECHO findings; five (10.4%) had

grossly dilated heart muscle disease/ cardiac wall hypokinesia; two (4.2%) had mitral valve stenosis with enlarged atria and intramural thrombi; one (2.1%) had mitral valve prolapse; one (2.1%) had atrial septal aneurysm and another one (2.1%) had infective endo-carditis (Figure 4).

Bilateral carotid-Doppler study: Thirty two of all stroke patients (40%) had bilateral carotid Doppler study done. Of these 32 patients 16 (50%) had normal bilateral carotid Doppler study findings; 12 (37.5%) had carotid arterosclerotic plaques without carotid stenosis; in three patients (9.3%) there was varied degree of internal carotid artery stenosis ranging from 20-60% and in one patient (3.1%) there was complete block; no-flow in the left internal carotid artery (Figure 5).

Hypercholesterolemia: A total of 52 patients (65%) had fasting lipid profile done. Ten (12.5%) patients had random lipid profile done and were therefore not included in analysis. Of the 52 patients who had fasting lipid profile done; 33(63.5%) had optimal or near optimal LDL cholesterol levels (<3.34 ml/l); 18(34.6%) had borderline high to very high LDL cholesterol levels LDL ≥ 3.36 ml/l. Only one patient (1.9%) had very high LDL cholesterol levels that is, ≥ 4.14 ml/l.

Figure 4
Observed 2D Echo-cardio graphic findings

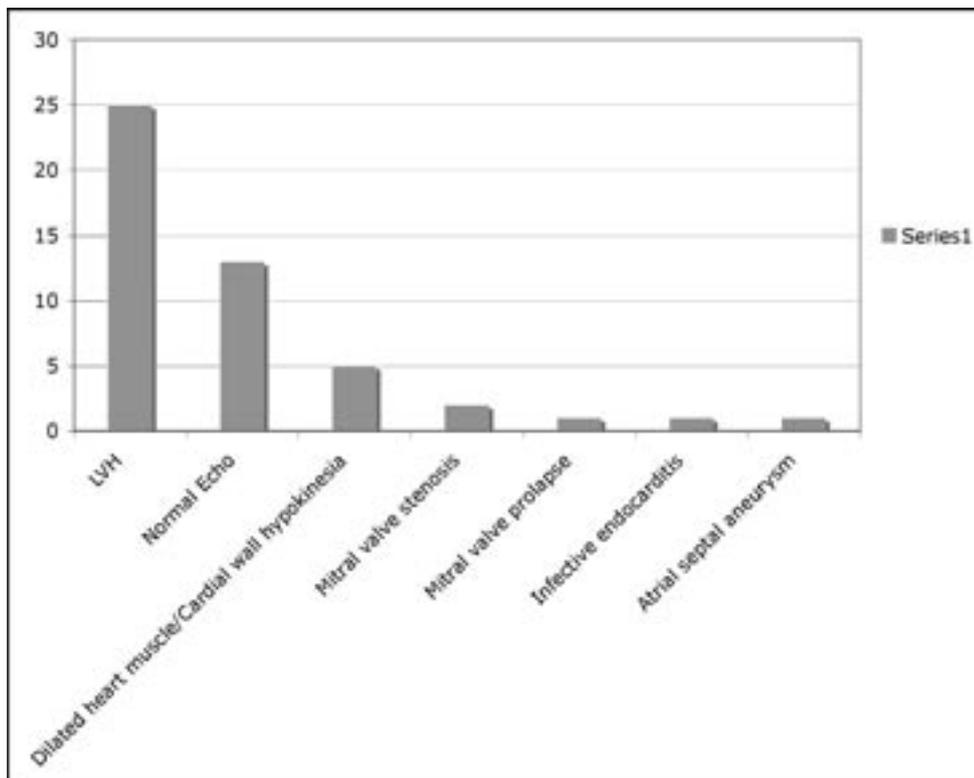
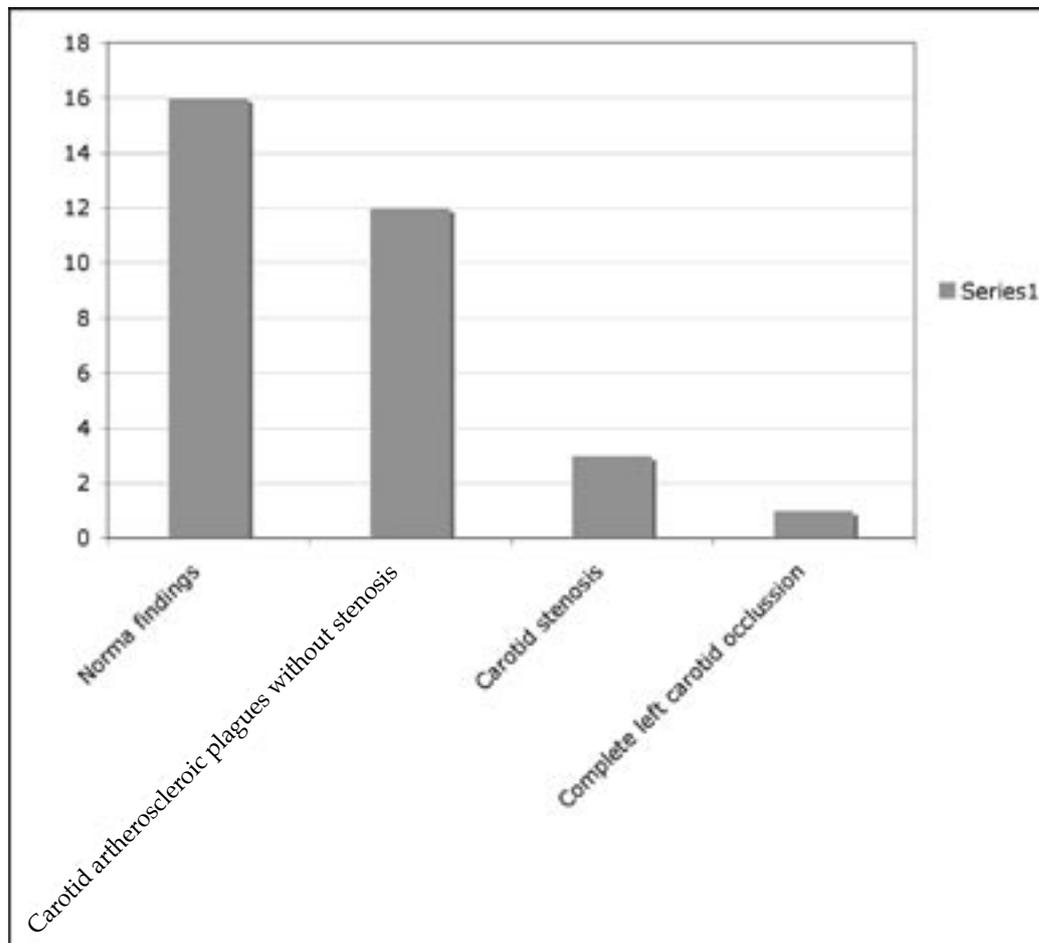


Figure 5
The bilateral carotid Doppler study findings



Cardiac arrhythmias: Ten (12.5%) patients had cardiac arrhythmias. In eight patients; arterial hypertension was co-morbidity. In two patients there was isolated cardiac arrhythmia.

Homo-cystenaemia: Only 19 patients (24%) with stroke had homocysteine levels done; of these seven (36.8%) had high homocysteine levels ≥ 15 .

HIV/AIDS: Two patients (2.5%) had HIV-AIDS. They all had ischaemic stroke in the brainstem; lacunae infarcts.

Anaemia: One patient (1.25%) had severe iron deficiency anaemia (haemoglobin 2.5 g/dl) as a sole co-morbidity. She was aged 45 years.

No risk factor/co-morbidity identified: In three patients (3.8%) no risk factor/ co-morbidity was identified as per file record. These included a 34 year old male, 38 and 40 year old females.

This being a retrospective study; history of smoking was not reliably recorded and hence the risk factor was not considered.

TOAST Classification of sub-type of ischaemic stroke vis-à-vis- risk factors observed: Data were reviewed to look at the different risk factors/ co-morbidities observed in ischaemic stroke as per The TOAST classification of the different ischaemic vascular territories. The following were observed (Figures 6, 7 and 8).

Figure 6

Number of patients with anterior circulation stroke *Vis-à-vis*- risk factors/ co-morbidities observed

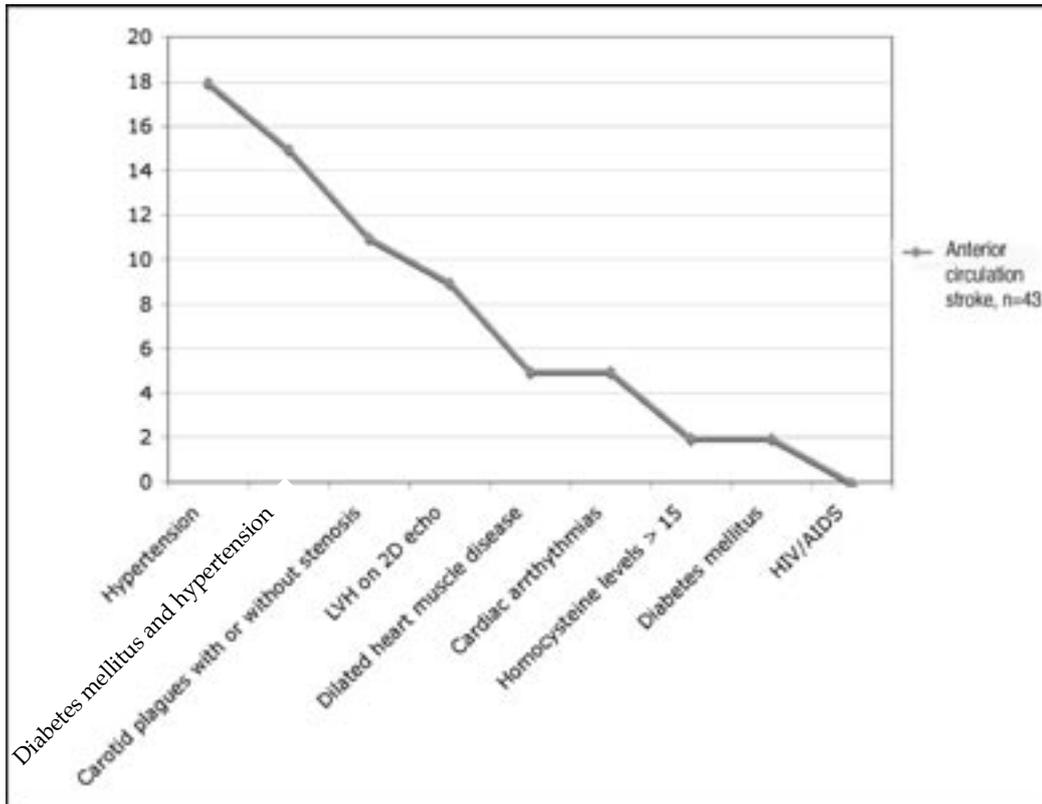


Figure 7

Number of patients with posterior circulation stroke *Vis-à-vis*- risk factors/ co-morbidities observed

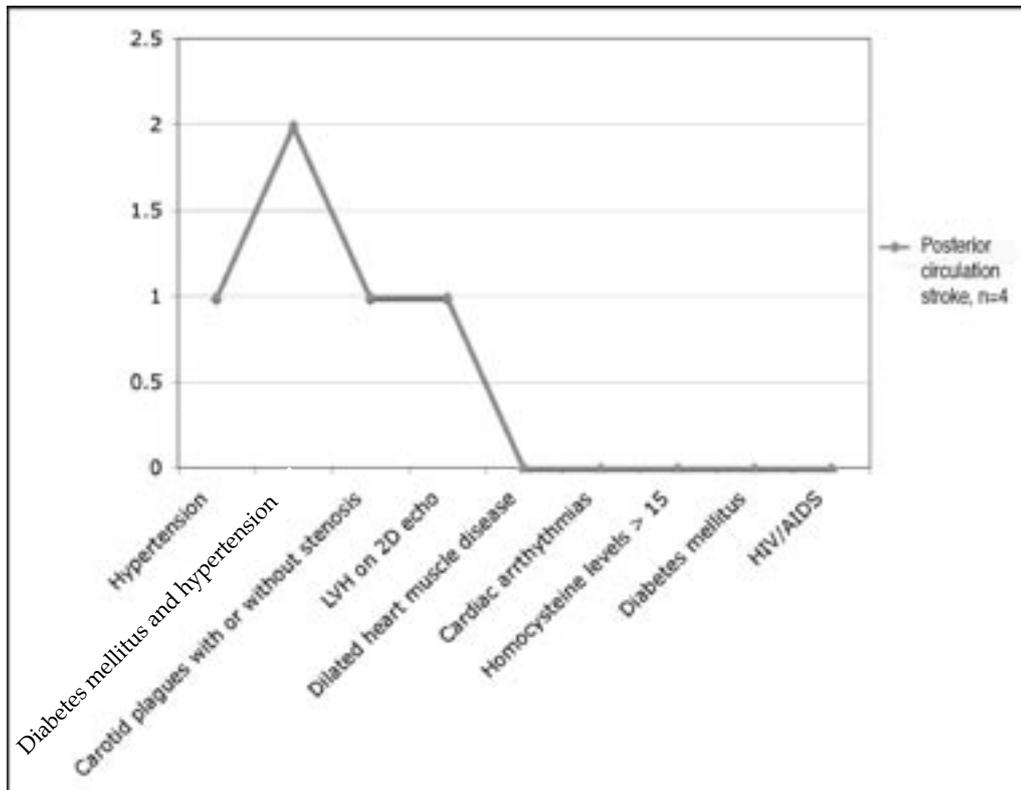
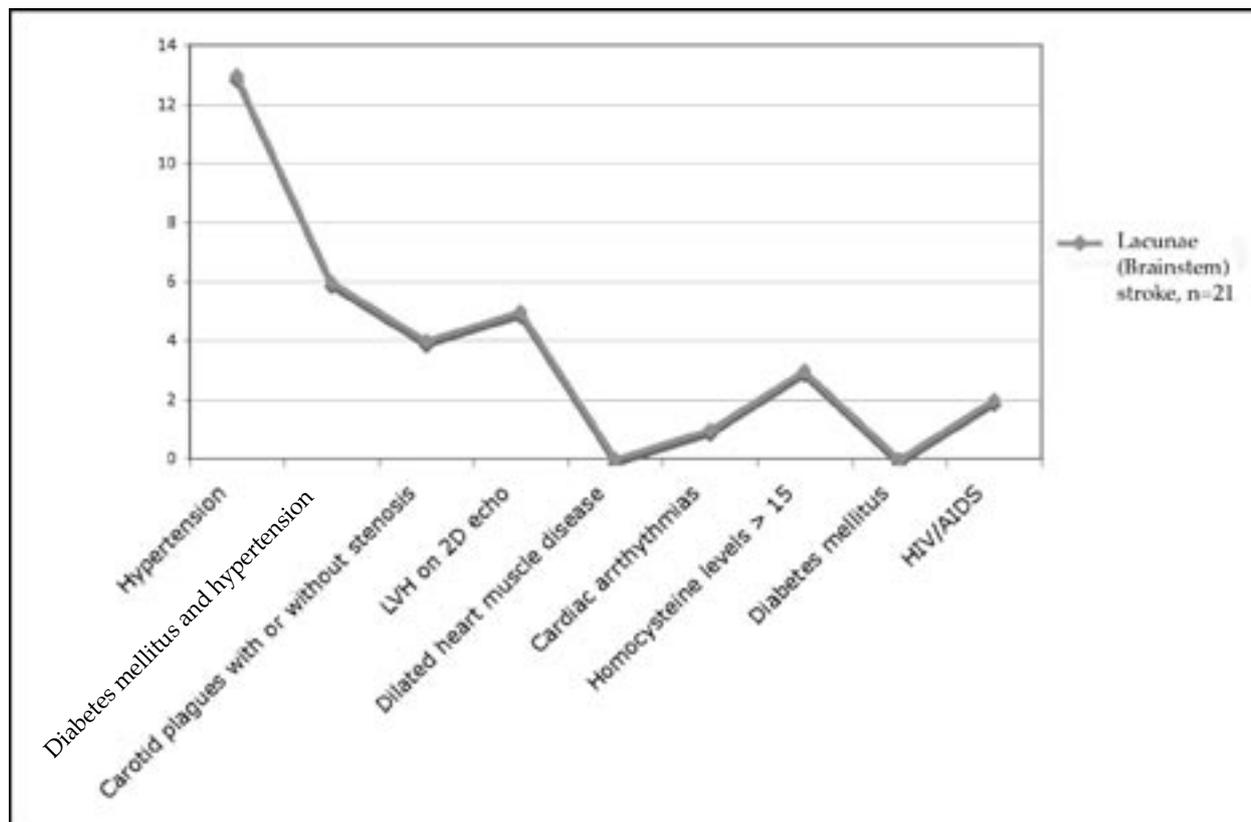


Figure 8

Number of patients with lacunae (brainstem) stroke Vis-à-vis- risk factors / co-morbidities observed



Duration of hospital stay: The mean duration of hospital stay was 12.5 days. Thirteen patients (16%) stayed in hospital for over 21 days. Hospital stay range was 22 to 70 days.

Outcome: Seventy five patients (93.8%) were discharged from hospital; four patients (5%) died while in hospital. All the four deaths were in patients with anterior circulation ischaemic stroke. One patient (1.25%) was transferred out on family request.

DISCUSSION

Stroke is increasingly becoming a significant health concern in the developing world (3, 16-18, 23, 25-27). Much emphasis has been put on infectious disease in health policy planning of developing countries. It is well to emphasize on infectious diseases as these are still the major killers. However, there is need to focus on non-infectious diseases such as stroke, epilepsy, movement disorders and metabolic syndromes amongst others. Data on these disorders in the developing world is scanty.

We carried out a hospital-based retrospective study to determine in-hospital point prevalence, observe the established risk factors / co-morbidities and pathological sub-types of stroke. Out of a total

of 2629 patients admitted during the study period, 80 patients had diagnosis of stroke based on clinical findings and CT/MRI scan report records on file. This gives an in-hospital period prevalence for stroke of 3042 per 100,000. This is much higher than other prevalence studies carried out in community surveys in Africa. The likely reason is that ours was a hospital based study in a tertiary centre therefore there was referral bias. In a community survey in AgriCort Health and Population Unit, a demographic surveillance site in rural South Africa where they investigated the prevalence of stroke survivors; a prevalence of 300 per 100,000 was found (3). Community based urban surveys in Nigeria gave period prevalence of between 58/100,000 and 70/100,000 (33).

There is need to undertake a community based stroke prevalence surveys in Kenya. It is interesting to note that community based stroke prevalence surveys in East Asia are much higher than those in Africa. The National Health Interview Survey in Taiwan conducted a house-hold survey in a three month period (Oct-Dec 1994) and identified 71 cases of stroke among a population of 11,925 surveyed; giving a point prevalence of 595/100,000 for all age groups; a prevalence of 1428/100,000 for persons over 35 years and a prevalence of 5080/100,000 for

persons over the age of 65 years (34). One would want to find out the reasons for these varied stroke prevalence rates in Africa compared to East Asia.

Arterial hypertension was observed to be the leading risk factor for both ischaemic and haemorrhagic stroke in our study. This compares with findings elsewhere (2, 32).

Stroke is associated with hypertension in several ways. These include issues of drug adherence, requisite long term medication and the fact that patients with hypertension are often asymptomatic. Studies done elsewhere indicate that nearly half of patients with hypertension do not take their medication regularly (15, 32). This study did not determine control and drug adherence of patients with hypertension. However, poorly controlled hypertension leads to complications such as hypertensive heart disease, left ventricular hypertrophy, arteriosclerosis and stroke. Health workers ought to stress to patients the significance of strict blood pressure control (15, 32).

Diabetes mellitus was the second most common observed risk factor in our patients. Poorly controlled diabetes has been shown to contribute to poor outcome in stroke patients (35). This study, however, did not look at control of diabetes mellitus. There is need for clinicians to emphasise early diagnosis and appropriate good control of diabetes mellitus.

Co-morbidities such as HIV/AIDS and homocystenaemia are emerging and should be sought in patients presenting with stroke. Ischaemic stroke was the most common pathological sub-type; seen in 85% of patients. Similar data is obtained from other studies (32). This, however, is contrary to what Matuja *et al* (2) found in Tanzania. It is not clear from the study findings why this was so.

Of the 68 patients with ischaemic stroke, 43 (63%) had anterior circulation territory ischaemia and four (5.9%) had posterior circulation territory ischaemia. These patients would be classified as having large artery, atherosclerosis (embolus/thrombus) as per TOAST classification of sub-types of acute ischaemic stroke (36). Twenty one patients (30.9%) had brain stem (lacunae) ischaemia. These patients would be classified as having small vessel occlusion as per TOAST classification (36).

It is crucial to evaluate patients and have a TOAST classification of acute ischaemic stroke sub-type because it has a prognostic basis. There is a trend towards increased risk of recurrent stroke in patients with anterior circulation infarct (37). All patients in our study, who died, had anterior circulation ischaemic stroke.

We looked at the various risk factors; co-morbidity vis-à-vis sub-types of ischaemic stroke as per TOAST classification that is, anterior circulation stroke, posterior circulation stroke and small vessel occlusion (lacunae) stroke; Figures 6, 7, 8 and no

statistical significant difference in frequencies was found.

Reviewing various other investigations done; 48 patients had 2D echo, 25 of whom had left ventricular hypertrophy, 13 had normal findings. Ten patients variously had dilated heart muscle disease, mitral stenosis, mitral valve prolapse and infective endocarditis on echo findings. This latter group of ten patients would be classified as having cardio embolism as per TOAST classification. Thirty two patients had bilateral carotid Doppler studies done. Sixteen of these patients (50%) had various degrees of atherosclerotic lesions varying from no stenosis to complete occlusion of the carotid arteries (Figure 5). These patients would fall under the category of large artery atherosclerosis in TOAST classification.

It would, however, be prudent to do a prospective study so that strict clinical evaluation coupled with neuro-imaging findings would result in an accurate TOAST classification of sub-types of acute ischaemic stroke. Patients with symptomatic carotid stenosis of recent origin have a high risk of early recurrence of stroke (38). Detailed history and appropriate clinical evaluation including carotid Doppler study is therefore necessary.

In patients with carotid stenosis of 50-69%; are symptomatic and certainly those with stenosis of $\geq 70\%$; consideration for endarterectomy is recommended because studies have shown it prevents stroke (39). The recommendation would depend on age, gender, type of symptoms e.g. TIAs, ocular (amourosis fugax), stroke and plaque surface morphology (40). Endarterectomy in patients with near occlusion is controversial. Studies have shown that endarterectomy does not prevent stroke in these patients.

Anti-platelets and statins are used in all patients with carotid plaques and or stenosis. Anti-coagulant use is restricted to patients with atrial fibrillation or mural thrombi (41). There is no doubt that hospital-based study is not the ideal in determining prevalence and incidence rates of stroke. We need to do community based studies in order to get accurate epidemiological data for stroke. This would aid in appropriate planning of preventive measures to curb the rising menace of stroke in the community. Community based studies must be done in accordance with strict criteria to enable our data be comparable to international data (42). Long hospital-stay of stroke patients is an added burden to the already scanty health resources in the developing countries.

In conclusion, ischaemic stroke is the most common pathological sub-type. Large-artery atherosclerosis is the most common sub-type of ischaemic stroke as per TOAST classification.

Hypertension and diabetes were the major risk factors observed for both ischaemic and haemorrhagic strokes. A prospective study would permit an appropriate risk analysis assessment for the various co-morbidities observed. There is an urgent need to do prospective case-control cohort studies to accurately classify etiology of ischaemic and haemorrhagic strokes.

Appropriately conducted community based studies to ascertain the prevalence and incidence of stroke is wanting in developing countries. Stroke, as a public health problem should be brought to the fore by clinicians, health institutions, medical schools and various governments. There must be a concerted multi-disciplinary approach to management of stroke and its attendant risk factors.

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